



November 27, 2019

TO: Republican Members, Committee on Energy and Commerce

FROM: Committee Minority Staff

RE: Hearing entitled “Flu Season: U.S. Public Health Preparedness and Response”

The Subcommittee on Oversight and Investigations will hold a hearing on Wednesday, December 4, 2019, at 10:30 a.m. in 2123 Rayburn House Office Building entitled “Flu Season: U.S. Public Health Preparedness and Response.”

I. WITNESSES

- Nancy Messonnier, M.D. (CAPT, USPHS, RET), Director, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services;
- Anthony S. Fauci, M.D., Director, National Institute for Allergy and Infectious Diseases, National Institutes of Health, U.S. Department of Health and Human Services;
- Robert Kadlec, M.D., M.T.M.&H, M.S., Assistant Secretary for Preparedness and Response, U.S. Department of Health and Human Services; and
- Peter Marks, M.D., Ph.D., Director, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, U.S. Department of Health and Human Services.

II. BACKGROUND

A. Overview of Seasonal Influenza in the United States

Influenza (the “flu”) is a contagious respiratory illness caused by different virus strains and can range in severity from mild to deadly. In both its seasonal and pandemic forms, the flu is an ongoing public health concern and is a leading cause of death in the United States.¹ The number of illnesses, hospitalizations, and deaths per year can vary depending on several factors, including but not limited to, the severity of the flu season, characteristics of the prevalent viruses, and the effectiveness of the vaccine. The Centers for Disease Control and Prevention (CDC) estimates that, on an annual basis since 2010, the flu has resulted in between 9.3 million and 49

¹ Seasonal flu is an outbreak that follows predictable seasonal patterns. Pandemic flu is a worldwide outbreak of a new form of flu virus, which can spread easily from person to person because most people have little to no immunity. Centers for Disease Control and Prevention (CDC), *How is Pandemic Flu Different from Seasonal Flu?* (last reviewed May 7, 2019), available at <https://www.cdc.gov/flu/pandemic-resources/basics/about.html>.

million illnesses, 140,000 and 960,000 hospitalizations, and 12,000 and 79,000 deaths.² As noted in CDC's 2020 Congressional Budget Justification, a 2007 study estimated that more than \$10 billion is spent each year in direct medical costs for hospitalizations and outpatient visits from seasonal flu-related complications.³

Although CDC estimates the number of flu-associated deaths, CDC does not calculate the exact number of individuals that die each year from the seasonal flu. The agency cannot calculate this number for a variety of reasons, including that: (1) states are not required to report individual seasonal flu cases or deaths of people aged 18 years and older to CDC; (2) many flu-related deaths, such as from pneumonia, may not include any mention of flu on the death certificate; (3) it can be difficult to identify which cases to include in an analysis since many patients (especially the elderly) may die from pneumonia unrelated to flu; and (4) most people who die from seasonal flu-related complications are not tested for flu or they seek medical care when flu can no longer be detected. Given the difficulties in calculating the precise number of flu-related deaths, researchers use a variety of modeling techniques to estimate deaths. CDC uses a mathematical model that is based on FluSurv-NET to estimate the annual number of flu-related deaths—previously, CDC estimated flu deaths using a statistical model of data on deaths with respiratory and circulatory causes.⁴

While the flu may result in death or hospitalization, most individuals who get the flu only have a mild illness and will recover in less than two weeks.⁵ Examples of flu-related complications include bronchitis, pneumonia, ear infections, sinus infections, and worsening of chronic health conditions. Those individuals that are at high risk for developing flu-related complications include, but are not limited to, children younger than five years of age, adults 65 years of age and older, pregnant women, residents of long-term care facilities, American Indians and Alaska Natives, and individuals with certain medical conditions.⁶ Although individuals aged 65 and older are more likely to receive the flu vaccine than younger adults, hospitalization rates for the flu are likely to be highest among the elderly. For example, for the 2017-2018 flu season, 37.1 percent of people aged 18 years and older received the vaccination—26.9 percent among adults between 18 and 49 years old and 59.6 percent of people aged 65 years and older received the vaccination.⁷ About 70 percent of the estimated hospitalizations and 90 percent of deaths for

² CDC, *Disease Burden of Influenza* (last reviewed Nov. 22, 2019), available at <https://www.cdc.gov/flu/about/burden/index.html>.

³ CDC, *FY 2020 Congressional Justification*, at 61 (2020), available at <https://www.cdc.gov/budget/documents/fy2020/fy-2020-cdc-congressional-justification.pdf>; See also Molinari, et al., *The annual impact of seasonal influenza in the US: measuring disease burden and costs*, VACCINE Volume 25 Issue 27 (Jun. 28, 2007).

⁴ CDC, *Frequently Asked Questions about Estimated Flu Burden* (last reviewed Nov. 5, 2018), available at <https://www.cdc.gov/flu/about/burden/faq.htm>.

⁵ CDC, *People at High Risk For Flu Complications* (last reviewed Aug. 27, 2018), available at https://www.cdc.gov/flu/about/disease/high_risk.htm.

⁶ *Id.*

⁷ CDC, *Estimates of Influenza Vaccination Coverage among Adults—United States, 2017-18 Flu Season* (last reviewed Nov. 5, 2018), available at <https://www.cdc.gov/flu/fluview/cov-1718estimates.htm#results>.

the 2017-2018 flu season, however, occurred in individuals aged 65 years and older.⁸ These statistics highlight that older adults are a particularly vulnerable population with respect to the flu.

Overall, seasonal flu has significant health and economic impacts, with a cumulative impact as serious as a pandemic. According to the World Health Organization (WHO), annual seasonal flu epidemics result in about three million to five million cases of severe illness and about 290,000 to 650,000 deaths worldwide, although the effects of seasonal flu in developing countries are not fully known.⁹ As noted in a 2012 report by the Center for Infectious Disease Research and Policy, “[t]hese figures indicate that the cumulative health impact of seasonal influenza over the last century rivals the potentially explosive, but time-limited, impact of the four pandemics of the past 100 years.”¹⁰

For the current influenza season, the U.S. is seeing more flu activity than normal at this point in the season, with 30 states already reporting activity — the most states reporting this early in a decade.¹¹ The overall hospitalization rate for the season is similar to rates at the same time in previous seasons.¹² The death rate attributable to pneumonia and influenza was below the epidemic threshold of six percent.¹³ As of November 16, 2019, there have been four pediatric flu deaths.¹⁴

B. Types of Influenza and Influenza Detection

The influenza virus is made up of single-stranded ribonucleic acid (RNA) segments that are coated by a nucleoprotein.¹⁵ The four types of influenza viruses (A, B, C, and D) are primarily distinguished by their different main nucleoproteins.¹⁶ Influenza types A, B, and C have the capacity to infect humans whereas influenza type D primarily infects cattle and is not known to infect or cause illness in humans.¹⁷ Influenza types A and B are the two main types of

⁸ CDC, *Estimated Influenza Illnesses, Medical Visits, Hospitalizations, and Deaths in the United States – 2017 – 2018 influenza season* (page last reviewed Nov. 22, 2019), available at <https://www.cdc.gov/flu/about/burden/2017-2018.htm>.

⁹ World Health Organization (WHO), Newsroom, Fact sheets, Detail, Influenza (Seasonal) (Nov. 6, 2018), available at [https://www.who.int/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)).

¹⁰ Center for Infectious Disease Research and Policy, University of Minnesota, *The Compelling Need for Game-Changing Influenza Vaccines: An Analysis of the Influenza Vaccine Enterprise and Recommendations for the Future*, at 11 (Oct. 2012).

¹¹ Gabrielle Masson, *US sees earliest flu season in 10 years*, Becker Hospital Review (November 22, 2019), available at <https://www.beckershospitalreview.com/quality/flu-activity-supasses-national-baseline-highest-of-the-season.html>.

¹² *Id.*

¹³ *Id.*

¹⁴ *Id.*

¹⁵ University of Pittsburgh Schools of the Health Sciences, *50-year-old flu virus model revamped, revealing pandemic prediction possibilities*, SCIENCE DAILY (Jul. 13, 2017), available at <https://www.sciencedaily.com/releases/2017/07/170713154853.htm>; Nara Lee, et al., *Genome-wide analysis of influenza viral RNA and nucleoprotein association*, NUCLEIC ACIDS RESEARCH Volume 45, Issue 15 (Sept. 6, 2017).

¹⁶ CDC, *Types of Influenza Viruses* (page last reviewed Nov. 18, 2019), available at <https://www.cdc.gov/flu/about/viruses/types.htm>.

¹⁷ *Id.*

viruses that cause seasonal epidemics and typically pose the most serious public health threat. Influenza type C infections are not believed to cause epidemics and instead typically cause mild respiratory illness.¹⁸

The CDC adheres to an internationally accepted naming convention for influenza viruses that was accepted by the WHO in 1979.¹⁹ Each influenza virus is named according to: (1) the antigenic type (*e.g.*, A, B, C); (2) the host of origin for viruses that did not originate in humans (*e.g.*, swine, chicken, etc. (no host of origin designation is provided for human-origin viruses)); (3) geographical origin (*e.g.*, Denver, Taiwan, etc.); (4) strain number (*e.g.*, 15, 7, etc.); (5) year of isolation (*e.g.*, 2009, etc.); and (6) the hemagglutinin (H) and neuraminidase (N) antigen in parentheses for influenza type A viruses (*e.g.*, (H1N1) (influenza types B and C do not receive these subtype classifications)).²⁰

Recently, influenza strains have grown increasingly complex and have been distributed more broadly across the globe. In February 2015, the WHO noted that the world needed to be concerned about the diversity and geographical distribution of influenza viruses:

The current global influenza situation is characterized by a number of trends that must be closely monitored. These include: an increase in the variety of animal influenza viruses co-circulating and exchanging genetic material, giving rise to novel strains. . . . The diversity and geographical distribution of influenza viruses currently circulating in wild and domestic birds are unprecedented since the advent of modern tools for virus detection and characterization. The world needs to be concerned.²¹

The news of this array of genetic forms of flu is partly a result of improved surveillance measures.²² Many scientists, however, believe that the pace of evolution in flu is speeding up because of human movement and trade along the Asian flyway, giving more opportunities for various types of flu to comingle, mix their RNA genetic material, and form novel strains.²³ This in turn is making it harder for scientists to predict which forms of flu are likely to hit human populations during certain seasons, accurately predict what type of vaccine is likely to be effective for that season, and anticipate the movement of flu viruses from wild birds to domestic fowl, fowl to humans, humans to swine, and swine back to humans. The consequences from the emergence of so many novel viruses “for animal and human health are unpredictable yet potentially ominous.”²⁴

¹⁸ *Id.*

¹⁹ *Id.*

²⁰ *Id.*

²¹ WHO, *Warning signals from the volatile world of influenza viruses* (Feb. 2015), available at <http://www.who.int/influenza/publications/warningsignals201502/en/>.

²² Lauren S. Polansky, et al., CDC, *Improved Global Capacity for Influenza Surveillance*, EMERGING INFECTIOUS DISEASES Volume 22, Number 6 (June 2016).

²³ Laurie Garrett, *The Year of the Flu*, COUNCIL ON FOREIGN RELATIONS (Feb. 4, 2015), available at <https://www.cfr.org/expert-brief/year-flu>.

²⁴ WHO, *supra* note 22.

Moreover, flu viruses constantly change through antigenic drift and antigenic shift.²⁵ Antigenic drift refers to small changes in the genes of flu viruses that happen continually over time as the virus replicates.²⁶ Antigenic shift occurs when there is an abrupt, significant change in the influenza A virus resulting in a new H and/or new H and N proteins. Because the H and N antigens can undergo antigenic shifts or drifts and mutate frequently, influenza type A typically causes the most severe outbreaks. Indeed, new influenza type A viruses are constantly emerging from animal reservoirs, and there has been a tenfold increase in the number of human infections with different novel influenza A viruses since the 1990s.²⁷ One specific subtype of influenza type A, H3N2, has a faster mutation rate than H1N1 or influenza B viruses, and this fast mutation rate can make it even more difficult to make an effective vaccine during some flu seasons.²⁸

Because of the potential for changes in the circulating flu viruses, close monitoring of flu viruses is required to evaluate the potential impact of the seasonal flu on public health. CDC uses different tests to characterize flu viruses, including genomic sequencing and Hemagglutinin Inhibition Assay (HAI/HI assay).²⁹ For samples collected and submitted to United States laboratories from October 1, 2017 to February 17, 2018, CDC has antigenically or genetically characterized 1,599 flu viruses, including 350 influenza A(H1N1)pdm09 viruses, 779 influenza A(H3N2) viruses, and 470 influenza B viruses.³⁰ For H3N2, the analysis for the 2017-2018 flu season “revealed extensive generic diversity with multiple clades/subclades co-circulating.”³¹

²⁵ CDC, *How the Flu Virus Can Change: “Drift” and “Shift,”* (page last reviewed Oct. 15, 2019), available at <https://www.cdc.gov/flu/about/viruses/change.htm>.

²⁶ *Id.*

²⁷ National Academies of Sciences, Engineering, Medicine, *Rapid Medical Countermeasure Response to Infectious Diseases, Workshop Summary*, at 48 (Oct. 12, 2015), available at <https://www.nap.edu/read/21809/chapter/6?term=1990#48>.

²⁸ Helen Branswell, *‘The problem child of seasonal flu’: Beware this winter’s virus*, STAT NEWS (Jan. 8, 2018), available at <https://www.statnews.com/2018/01/08/flu-virus-h3n2/>.

²⁹ Laurie Garrett, *The Year of the Flu*, COUNCIL ON FOREIGN RELATIONS (Feb. 4, 2015), available at <https://www.cfr.org/expert-brief/year-flu>; Hearing before the U.S. House of Representatives, Committee on Energy and Commerce, “U.S. Public Health Preparedness for Seasonal Influenza: Has the Response Improved?” (Nov. 19, 2015).

³⁰ *Id.* Some researchers have found that the H3N2 virus poses significant health risks and results in more fatalities and hospitalizations than other influenza viruses. Dan Gray, *2018 Flu Season Off to a Strong, Potentially Dangerous Start*, HEALTHLINE (Jan. 3, 2018), available at <https://www.healthline.com/health-news/2018-flu-season-potentially-dangerous-start#1>.

³¹ Laurie Garrett, *supra* note 30.

C. Seasonal Flu Vaccine: Development and Effectiveness

i. Seasonal Influenza Vaccine Development

The flu vaccine must be reformulated on an annual basis to protect against strains expected to be most prevalent that year since circulating flu virus strains constantly change.³² Each year, public health experts, including those from the Food and Drug Administration (FDA), WHO, and CDC, study flu virus samples and global disease patterns to identify virus strains likely to cause the most illness during the upcoming season.³³ In collaboration with other partners, WHO recommends the specific vaccine viruses that should be included in the next season's flu vaccines in the northern hemisphere every February.

For the 2019-2020 flu season, the WHO made recommendations for three of the four components of the flu vaccine on February 21, 2019; however, "[t]he decision on the A(H3N2) component was postponed to allow more time to better understand the distribution and proportions of recently circulating antigenically and genetically diverse A(H3N2) viruses and to develop and fully characterize appropriate candidate vaccine viruses until March 21, 2019."³⁴ The FDA then selects the strains for inclusion in the annual flu virus that is sold and distributed in the United States based on that information and the recommendations of FDA's Vaccines and Related Biological Products Advisory Committee (VRBAC).³⁵

Most flu vaccines are injectable and include inactivated flu vaccines and recombinant flu vaccines.³⁶ Typically, the flu vaccine protects against three or four different flu viruses. There are three different production technologies approved by the FDA for injectable flu vaccines: (1) egg-based flu vaccine; (2) cell-based flu vaccine; and (3) recombinant flu vaccine. The egg-based manufacturing process, which has been used for more than seventy years and takes about 22 to 24 weeks to produce, is the most common way that flu vaccines are manufactured in the United States. The cell-based production process, approved by FDA in 2012, takes about 16 to 17 weeks to manufacture the vaccine. The recombinant flu vaccine manufacturing process, approved by FDA in 2013, can produce flu vaccines in the shortest amount of time at about 12 to 15 weeks.

³² CDC, *Selecting Viruses for the Seasonal Influenza Vaccine* (last reviewed Sept. 4, 2018), available at <https://www.cdc.gov/flu/about/season/vaccine-selection.htm>.

³³ In the northern hemisphere, seasonal influenza may begin as early as August and generally diminishes by April. Typically, influenza activity peaks between December and February in the United States but may peak later in the season. CDC, *2015-2016 Estimated Influenza Illnesses, Medical Visits, and Hospitalizations Averted by Vaccination in the United States* (last reviewed Nov. 6, 2019), available at <https://www.cdc.gov/flu/about/disease/2015-16.htm>.

³⁴ WHO, Addendum to the recommended composition of influenza virus vaccines for use in the 2109-2020 northern hemisphere influenza season (Mar. 21, 2019), available at https://www.who.int/influenza/vaccines/virus/recommendations/201902_recommendation_addendum.pdf?ua=1.

³⁵ Robert Lowes, *First Quadrivalent Flu Vaccine Approved, Debuts Fall 2013*, MEDSCAPE (Mar. 1, 2012), available at <https://www.medscape.com/viewarticle/759517>.

³⁶ Immunization Action Coalition, *Influenza Vaccine Products for the 2017-2018 Influenza Season* (last visited Nov. 26, 2019), available at <http://www.immunize.org/catg.d/p4072.pdf>.

In 2003, FDA approved a trivalent nasal spray flu vaccine—called FluMist—that includes a live attenuated flu vaccine for certain ages.³⁷ In 2012, FDA approved FluMist Quadrivalent.³⁸ In 2014, CDC’s Advisory Committee on Immunization Practices (ACIP) made a preferential recommendation for FluMist in healthy children ages 2 to 8, because it seemed to offer better protection.³⁹ However, it reversed the decision in 2015 because of disappointing performance against the 2009 H1N1 strain.⁴⁰ In addition, because data from observational studies showed low effectiveness of FluMist Quadrivalent against a specific strain of the flu virus in the United States during the 2013-2014 and 2015-2016 flu seasons, ACIP did not recommend that the live attenuated vaccine be used by individuals for the past few years.⁴¹ In February 2018, ACIP recommended that the live attenuated flu vaccine be included on the 2018-2019 flu vaccination schedule for individuals for whom it is appropriate.⁴²

For the 2019-2020 flu season, manufacturers estimate that they will provide as many as 162 million to 169 million doses of injectable vaccine in the United States.⁴³ For the 2019-2020 season, manufacturers will produce both trivalent (three-component) and quadrivalent (four-component) flu vaccines. About 81 percent of the projected vaccine supply will be quadrivalent, and the remaining supply will be trivalent, “including the high dose and adjuvanted vaccines, as well as one brand of standard-dose inactivated vaccine.”⁴⁴ According to the CDC, about 82 percent of the vaccine supply for the 2019-2020 flu season will be manufactured using egg-based manufacturing technology and the remaining vaccines will be produced using cell-based and recombinant technology.⁴⁵

³⁷ U.S. Food and Drug Administration (FDA), *FDA Information Regarding FluMist Quadrivalent Vaccine* (last updated Jan. 26, 2018), available at <https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm508761.htm>.

³⁸ *Id.*

³⁹ Center for Infectious Disease Research and Policy (CIDRAP) News, *CDC vaccine panel brings back FluMist for 2018-19 season* (Feb. 21, 2018), available at <http://www.cidrap.umn.edu/news-perspective/2018/02/cdc-vaccine-panel-brings-back-flumist-2018-19-season>.

⁴⁰ *Id.*

⁴¹ CDC, *Prevention and Control of Seasonal Influenza with Vaccines, Recommendations of the Advisory Committee on Immunization Practices—United States, 2016-17 Influenza Season* (Aug. 26, 2016), available at https://www.cdc.gov/mmwr/volumes/65/rr/rr6505a1.htm#T1_down.

⁴² Molly Walker, *ACIP Reinstates FluMist for 2018-2019 Flu Season*, MEDSCAPE (Feb. 21, 2018), available at <https://www.medpagetoday.com/meetingcoverage/acip/71298>.

⁴³ CDC, *Seasonal Influenza Vaccine Supply for the U.S. 2019-2020 Influenza Season*, (last updated Sept. 24, 2019), available at <https://www.cdc.gov/flu/prevent/vaxsupply.htm>.

⁴⁴ *Id.*

⁴⁵ *Id.*

ii. Seasonal Influenza Prevention and Vaccine Effectiveness

The primary method for preventing flu is annual vaccination. According to the CDC's 2020 Congressional Budget Justification, vaccination prevented approximately 5.3 million flu illnesses, 2.6 million flu-associated medical visits, and 84,700 flu-associated hospitalizations during the 2016-2017 flu season.⁴⁶ Similarly, a 2015 study published in the journal *Vaccine* showed that the seasonal flu vaccine prevented more than 40,000 flu-associated deaths in the United States from 2005-2006 through 2013-2014.⁴⁷ Likewise, according to a 2017 study published by the CDC in the journal *Pediatrics*, the flu vaccine reduced the risk of flu-associated death by half for children with underlying high-risk medical conditions and by nearly two-thirds for healthy children.⁴⁸

Indeed, research indicates that even if the flu vaccine fails to protect an individual against being infected with the flu, the vaccine may help reduce severe outcomes.⁴⁹ According to CDC estimates, approximately 74 percent of flu-associated deaths in children in the 2017-2018 flu season occurred in children who were not vaccinated.⁵⁰ Likewise, a 2017 study by the CDC showed that receiving the flu vaccine reduced severe outcomes in hospitalized patients by reducing deaths, reducing intensive care unit (ICU) admissions, reducing ICU length of stay, and reducing overall duration of hospitalization among hospital patients.⁵¹ The study found that vaccinated adults were 52 to 70 percent less likely to die than unvaccinated flu-hospitalized patients and experienced additional benefits.⁵²

CDC estimates the effectiveness of the flu vaccine every year, and by effectiveness, CDC means the rate at which the vaccine prevents a person from getting sick with the flu and going to the doctor (the effectiveness rate does not, however, account for other potential benefits from receiving the flu vaccine such as helping reduce severe outcomes if an individual gets the flu).⁵³ Recent studies show that seasonal flu vaccination typically has an effectiveness rate in the range of 40 to 60 percent.⁵⁴ According to CDC, the overall, adjusted vaccine effectiveness estimates for flu seasons from 2005 to 2018 ranged from 10 to 60 percent.⁵⁵

⁴⁶ CDC, *FY 2020 Congressional Budget Justification*, *supra* note 3, at 62.

⁴⁷ Ivo Foppa, et al., *Deaths averted by influenza vaccination in the U.S. during the seasons 2005/06 through 2013/14*, *VACCINE* Volume 33 (June 12, 2015), available at www.sciencedirect.com/science/article/pii/S0264410X15002315.

⁴⁸ CDC, *CDC Study Finds Flu Vaccine Saves Children's Lives* (Apr. 3, 2017), available at <https://www.cdc.gov/media/releases/2017/p0403-flu-vaccine.html>.

⁴⁹ *Id.*

⁵⁰ CDC, *Estimates of Flu Vaccination Coverage among Children – United States, 2017-18 Flu Season* (last reviewed Oct. 5, 2018), available at <https://www.cdc.gov/flu/fluview/coverage-1718estimates-children.htm>.

⁵¹ CDC, *New CDC Study Shows Flu Vaccine Reduces Severe Outcomes in Hospitalized Patients* (May 25, 2017).

⁵² *Id.*

⁵³ CDC, *Summary of the 2017-2018 Influenza Season* (last reviewed Sept. 5, 2019), available at <https://www.cdc.gov/flu/about/season/flu-season-2017-2018.htm>.

⁵⁴ CDC, *Vaccine Effectiveness: How Well Do the Flu Vaccines Work?* (last reviewed Oct. 12, 2018), available at <https://www.cdc.gov/flu/vaccines-work/vaccineeffect.htm>.

⁵⁵ CDC, *Past Seasons Vaccine Effectiveness Estimates* (last reviewed Apr. 5, 2019), available at <https://www.cdc.gov/flu/vaccines-work/past-seasons-estimates.html>.

***CDC's Adjusted Vaccine
Effectiveness Estimates⁵⁶***

Year	Adjusted Overall Vaccine Effectiveness
2004-2005	10%
2005-2006	21%
2006-2007	52%
2007-2008	37%
2008-2009	41%
2009-2010	56%
2010-2011	60%
2011-2012	47%
2012-2013	49%
2013-2014	52%
2014-2015	19%
2015-2016	48%
2016-2017	40%
2017-2018	38%
2018-2019	29%

Vaccine effectiveness can differ depending on the age of the individual that received the vaccination. For example, for the 2018-2019 flu season, the vaccine was 29 percent effective for all age groups—49 percent effective for individuals aged 6 months to 8 years, 6 percent effective for individuals aged 9 to 17 years, 25 percent effective for individuals aged 18 to 49 years, 12 percent effective for individuals 50 to 64 years, and 12 percent effective for people aged 65 years and older.⁵⁷

Moreover, vaccine effectiveness also differs across different subtypes of flu. Research shows that the flu vaccine typically is more effective against influenza B and influenza A(H1N1) viruses than influenza A(H3N2) viruses.⁵⁸ Some researchers have raised concerns about the decline in effectiveness of the annual flu vaccine, especially for the H3N2 virus.⁵⁹ A 2016 meta-analysis of 56 past studies published in PubMed and Embase found that, on average, the seasonal flu vaccine was 33 percent effective against the H3N2 virus, 54 percent effective against influenza B, 61 percent effective against the H1N1pdm09 virus, and 67 percent effective against H1N1.⁶⁰ During the 2018-2019 flu season in the United States, CDC data shows that while the

⁵⁶ CDC, *Seasonal Flu Vaccine Effectiveness Studies* (last reviewed Nov. 5, 2019), available at <https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm>.

⁵⁷ CDC, Influenza (Flu), Seasonal Influenza, Flu Vaccines Work, Vaccine Effectiveness Studies, US Flu VE Data for 2018-2019 (last updated on Sept. 10, 2019), available at <https://www.cdc.gov/flu/vaccines-work/2018-2019.html>.

⁵⁸ CDC, *Vaccine Effectiveness—How Well Does the Flu Vaccine Work?* (last updated Oct. 12, 2018), available at <https://www.cdc.gov/flu/vaccines-work/vaccineeffect.htm>.

⁵⁹ Nicholas C. Wu, *A structural explanation for the low effectiveness of the seasonal influenza H3N2 vaccine*, PLOS PATHOGENS (Oct. 23, 2017), available at <http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1006682>.

⁶⁰ Edward A. Belongia, et al., *Variable influenza vaccine effectiveness by subtype: a systematic review and meta-analysis of test-negative design studies*, THE LANCET Volume 16 (Aug. 2016); See also Sarah Zhang, *Scientists*

flu vaccine had an overall vaccine effectiveness rate of 29 percent, vaccine effectiveness for all ages was 9 percent against type A(H3N2) viruses and 44 percent against influenza A(H1N1)pdm09 viruses.⁶¹

There are many different factors that may contribute to reduced vaccine effectiveness for the flu, including but not limited to: (1) antigenic differences between the circulating strain and the strain used to create the vaccine caused by antigenic drift and antigenic shift; (2) egg adaptation; and (3) other factors such as immune history⁶² and some individuals potentially requiring a higher amount of certain antigens, such as H3N2, to elicit a proper immune response to that particular strain of the flu.

The protective benefit from receiving the flu vaccine typically is decreased if the primary circulating flu viruses are different from the viruses that were used to make the vaccine for that season. As previously mentioned, flu viruses are continuously changing through antigenic drift and antigenic shift, and these changes can therefore impact the efficacy of the seasonal flu vaccine if the majority of the circulating viruses become different than those used for the vaccine. Even if antigenic drift occurs, however, the vaccine may provide protective benefit if the circulating flu virus is only mildly or moderately different than the virus used for the vaccine. If the small genetic changes that occur through antigenic drift accumulate over time and result in a virus that looks different to a person's immune system, the antibodies created against older viruses may no longer recognize the "newer" virus, and the person may no longer be protected.⁶³

While vaccine effectiveness is generally interpreted in the context of vaccine match/mismatch to circulating strains that have mutated to explain reduced protection, egg adaptation may also contribute to lower effectiveness of the vaccine—especially for certain strains of the virus such as H3N2.⁶⁴ More specifically, as human flu viruses adapt to grow in eggs during the manufacturing process, genetic changes may occur in the viruses referred to as "egg-adapted changes."⁶⁵ These egg-adapted changes can have important consequences for an individual's immune response to vaccination such as causing an individual to produce antibodies that are less effective at preventing illness caused by the specific flu viruses in circulation.⁶⁶

Found a Flu Vaccine – Now They Have to Fix It, WIRED (Oct. 9, 2015), available at <http://www.wired.com/2015/10/scientists-pinpoint-flu-vaccine-flaw-h3n2/>.

⁶¹ CDC, *US Flu VE Data for 2018-2019* (last reviewed Nov. 6, 2019), available at <https://www.cdc.gov/flu/vaccines-work/2018-2019.html>.

⁶² A recent study found that immune history with the influenza influences an individual's response to the flu vaccine. Matt Wood, *Immune history influences effectiveness of flu vaccine, study finds*, UCHICAGO NEWS (Feb. 20, 2018), available at <https://news.uchicago.edu/article/2018/02/20/immune-history-influences-effectiveness-flu-vaccine-study-finds>.

⁶³ CDC, *How the Flu Virus Can Change: "Drift" and "Shift,"* (last reviewed Oct. 15, 2019), available at <https://www.cdc.gov/flu/about/viruses/change.htm>.

⁶⁴ Nicholas C. Wu, *supra* note 62.

⁶⁵ CDC, *Antigenic Characterization* (last reviewed Oct. 15, 2019), available at <https://www.cdc.gov/flu/professionals/laboratory/antigenic.htm>.

⁶⁶ CDC, *Cell-Based Flu Vaccines* (last updated Oct. 11, 2019), available at <https://www.cdc.gov/flu/prevent/cell-based.htm>.

In 2014, a study funded by the Canadian Institutes of Health Research found that, during the 2012-2013 flu season, the low vaccine effectiveness was related to mutations in the egg-adapted H3N2 vaccine strain rather than antigenic drift in circulating viruses.⁶⁷ Likewise, for the 2017-2018 flu season, some experts expressed concern that the flu vaccine's reduced effectiveness against H3N2 may be caused in part by egg adaptation.⁶⁸ According to a February 15, 2018 statement by former FDA Commissioner Scott Gottlieb, M.D., the commonly used egg-based manufacturing process may not have produced a vaccine that was as effective against H3N2 as the cell-based manufacturing process:

A preliminary analysis of CMS data indicates that this year, the cell-based influenza vaccine appears to have somewhat better effectiveness in preventing influenza than the egg-based vaccine. Scientists at the FDA, CDC, and NIH are working diligently to fully understand the basis for this finding, so that all of next year's vaccines can provide better protection in preventing the flu. Better understanding why the cell-based vaccine offered better protection against H3N2 this season, when compared to the egg-based vaccine, may offer important clues to help improve the production of a more effective H3N2 vaccine for next season.⁶⁹

Similarly, CDC also recently said "we're hoping this year to find out whether or not there's a performance difference between cell-based vaccines and the egg-based vaccines."⁷⁰

On February 26, 2018, Dr. Gottlieb indicated that the FDA did not believe that the reduced effectiveness of the 2017-2018 seasonal vaccine against H3N2 was caused by public health authorities choosing the wrong strain of H3N2 when starting the process of making the 2017-2018 seasonal flu vaccine. Dr. Gottlieb stated, "so far the data we have suggests that the viruses provided by reference laboratories to manufacturers to make this year's vaccines do reasonably match the circulating flu strains that are causing most of the illnesses."⁷¹ Dr. Gottlieb provided several reasons that might explain the limited effectiveness of the 2017-2018 seasonal flu vaccine against H3N2:

One theory is that people might require a higher amount of H3N2 antigen to elicit a proper immune response to that particular strain of influenza. As I noted previously, the work conducted with CMS shows a preliminary finding that

⁶⁷ Danuta Skowronski, et al., *Low 2012-13 Influenza vaccine Effectiveness Associated with Mutation in the Egg-Adapted H3N2 Vaccine Strain Not Antigenic Drift in Circulating Viruses*, PLOS (Mar. 25, 2014), available at <http://journals.plos.org/plos.org/plosone/article?id=10.1371/journal.pone0092153>.

⁶⁸ Lisa Schnirring, University of Minnesota, Center for Infectious Disease Research and Policy, *WHO changes 2 strains for 2018-19 flu vaccine* (Feb. 22, 2018), available at <http://www.cidrap.umn.edu/news-perspective/2018/02/who-changes-2-strains-2018-19-flu-vaccine>.

⁶⁹ FDA, *Statement from FDA Commissioner Scott Gottlieb, M.D. on the efficacy of the 2017-2018 influenza vaccine* (Feb. 15, 2018), available at <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm597077.htm>.

⁷⁰ Maggie Fox, *Why next year's flu vaccine will be lousy, too*, NBC NEWS (Feb. 23, 2018), available at <https://www.nbcnews.com/health/health-news/why-next-year-s-flu-vaccine-will-be-lousy-too-n850641>.

⁷¹ FDA, *Statement from FDA Commissioner Scott Gottlieb, M.D., on FDA's ongoing efforts to help improve effectiveness of influenza vaccines* (Feb. 26, 2018), available at <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm598317.htm>.

suggests the cell-based influenza vaccine might be somewhat more effective than the egg-based vaccine. We are working to follow up on that finding. We're also combing through the data to see if there are other reasons for why this season's vaccines were less effective against H3N2.⁷²

The FDA anticipates that by better understanding why the effectiveness of the flu vaccine tends to be lower against H3N2, FDA can hopefully enhance vaccine effectiveness.

iii. Vaccine Coverage

Since 2010, ACIP has recommended annual vaccinations for everyone aged six months or older.⁷³ From the 2010-2011 to 2016-2017 flu seasons, an average of 56.5 percent of children (aged six months to 17 years) and 41.7 percent of adults were vaccinated each year.⁷⁴ Data from the 2015-2016 season showed that 59.3 percent of children and 41.7 percent of adults were vaccinated.⁷⁵ For 2016-2017 season, 59 percent of children and 43.3 percent of adults were vaccinated.⁷⁶ For 2017-2018 season, 57.9 percent of children⁷⁷ and 37.1 percent of adults were vaccinated.⁷⁸ For the 2018-2019 season, 62.6 percent of children and 45.3 percent of adults were vaccinated.⁷⁹

The Department of Health and Human Services (HHS) supports efforts to increase annual vaccination and continuously engages in efforts to improve public awareness and provider knowledge about flu and the importance of vaccination.⁸⁰ As part of the Healthy People 2020 initiative, HHS has set a goal for states to vaccinate 70 percent of their population. According to experts, vaccination rates need to be generally above 70 percent for “herd immunity” effects—which limit the spread and protect those without immunity—to become apparent.

On February 26, 2019, Republican leaders of the Committee sent a letter to CDC Director, Dr. Robert Redfield, requesting a briefing on questions regarding flu vaccination coverage for seniors, and whether a preferential recommendation from ACIP for vaccinating adults 65 years of age and older with a high-dose (Fluzone HD) or an adjuvanted (FLUAD) influenza vaccine could reduce deaths and hospitalizations or even improve vaccination

⁷² *Id.*

⁷³ CDC, *FY 2018 Congressional Budget Justification*, at 18, available at

<https://www.cdc.gov/budget/documents/fy2018/fy-2018-cdc-congressional-justification.pdf>.

⁷⁴ CDC, *Flu Vaccination Coverage, United States, 2016-17 Influenza Season* (last updated Sept. 28, 2017), available at <https://www.cdc.gov/flu/fluview/coverage-1617estimates.htm>.

⁷⁵ *Id.*

⁷⁶ *Id.*

⁷⁷ CDC, *Estimates of Flu Vaccination Coverage among Children – United States, 2017-18 Flu Season* (last reviewed Sept. 27, 2018), available at <https://www.cdc.gov/flu/fluview/coverage-1718estimates-children.htm#results>.

⁷⁸ CDC, *Estimates of Influenza Vaccination Coverage among Adults – United States, 2017-18 Flu Season* (last reviewed Nov. 5, 2018), available at <https://www.cdc.gov/flu/fluview/coverage-1718estimates.htm#results>.

⁷⁹ CDC, *Flu Vaccination Coverage, United States, 2018-19 Influenza Season* (last reviewed Sept. 26, 2019), available at <https://www.cdc.gov/flu/fluview/coverage-1819estimates.htm#results>.

⁸⁰ CDC, *FY 2018 Congressional Budget Justification*, at 46, available at <https://www.cdc.gov/budget/documents/fy2018/fy-2018-cdc-congressional-justification.pdf>.

coverage.⁸¹ On March 11, 2019, subject matter experts from the CDC briefed Minority Committee staff in response to the letter. CDC maintained that the amount of information concerning both Fluzone and FLUAD did not rise to a level of ACIP making a preference recommendation. CDC during the briefing indicated that a \$10 million increase for the influenza program could be used to examine out-of-the-box solutions to improving vaccination rates for seniors as well as the rest of the U.S. population.

D. Development of a Universal Flu Vaccine

One long-term goal to improve preparedness for and response to the flu is to develop a universal vaccine that would provide long-lasting immunity against multiple strains of the flu. The goal is to eliminate the need for individuals to receive an annual seasonal flu vaccine and to provide protection against newly emerging flu strains. The Biomedical Advanced Research and Development Authority (BARDA) within the Office of the Assistant Secretary for Preparedness and Response (ASPR) in HHS is coordinating a broad-interagency partnership to support the development of improved flu vaccines, including a universal flu vaccine.⁸² In June 2017, the National Institute of Allergy and Infectious Disease (NIAID) held a workshop entitled “Pathway to a Universal Influenza Vaccine” to identify and develop criteria that would define a universal flu vaccine, discuss knowledge gaps in the search for this vaccine, and to identify research strategies to address these gaps.⁸³ Following the workshop, NIAID published a strategic plan in February 2018 to “reinvigorate pursuit of a universal influenza vaccine.”⁸⁴

E. Pandemic Influenza

A flu pandemic can occur when a novel, non-human flu virus becomes able to spread efficiently through human-to-human transmission. The viruses circulate in birds or other animals, so there is little to no immunity against these viruses among people. According to CDC, pandemics rarely occur, and past pandemics include the 2009 Pandemic (H1N1 virus), the 1968 Pandemic (H3N2 virus), the 1957-1958 Pandemic (H2N2 virus), and the 1918 Pandemic (H1N1 virus).⁸⁵

⁸¹ Letter from Hon. Greg Walden, Republican Leader, H. Comm. on Energy & Commerce, et al., to Dr. Robert R. Redfield, Director, CDC (Feb. 26, 2019), *available at* <https://republicans-energycommerce.house.gov/wp-content/uploads/2019/02/02-26-19-Letter-to-CDC-on-flu-vaccination.pdf>.

⁸² CDC, *Influenza Vaccine Advances* (last updated Sept. 16, 2019), *available at* <https://www.cdc.gov/flu/prevent/advances.htm>.

⁸³ National Institutes of Health, National Institute of Allergy and Infectious Disease, *Experts Outline Pathway to a Universal Influenza Vaccine* (Oct. 17, 2017), *available at* <https://www.niaid.nih.gov/news-events/experts-outline-pathway-universal-influenza-vaccine>.

⁸⁴ Emily J. Erbelding, et al., *A Universal Influenza Vaccine: The Strategic Plan for the National Institute of Allergy and Infectious Diseases* (Mar. 2018).

⁸⁵ CDC, *Past Pandemics* (last reviewed Aug. 10, 2018), *available at* <https://www.cdc.gov/flu/pandemic-resources/basics/past-pandemics.html>.

HHS maintains a *Pandemic Influenza Plan*, which was developed in 2005.⁸⁶ The Committee wrote to HHS in April 2017 asking about the status of the updated plan.⁸⁷ HHS subsequently released the updated plan in June 2017.⁸⁸ The *Pandemic Influenza Plan* acts “as a blueprint for all HHS pandemic influenza preparedness planning and response activities.”⁸⁹ In the 2017 update, HHS notes that one of the improvements in the agency’s preparedness and response activities for pandemic flu over the past decade is that “HHS efforts in pandemic influenza preparedness now are closely aligned with seasonal influenza activities, harnessing expanded surveillance, laboratory, vaccine, and antiviral drug resistance monitoring capacity.”⁹⁰ According to the 2017 update:

[T]he continually changing nature of influenza viruses that can lead to mismatches between vaccine strains and circulating viruses, as seen during the 2014-2015 influenza season, remind us that pandemic and seasonal influenza planning and improvement efforts are interdependent. Both rely on a strong and sustainable public health system infrastructure that can rapidly detect, and respond to, changes in circulating influenza viruses. Many of the activities that HHS and its partners undertake each year to understand and mitigate the impact of seasonal influenza are critical to a pandemic response both domestically and globally.⁹¹

F. Improvements in U.S. Response to Seasonal Influenza and the 2019 Executive Order

After the 2014-2015 vaccine mismatch, then-HHS Secretary Sylvia Burwell, through her counselors, requested that HHS experts recommend actions to mitigate the seasonal flu mismatch problem. On May 6, 2015, a memorandum of flu process improvements was sent to Secretary Burwell. In November 2015, HHS held a table top exercise with HHS agencies and vaccine manufacturers, to solicit their individual opinions. On November 19, 2015, the Subcommittee held a hearing on whether the public health response to seasonal flu had improved.⁹²

On March 8, 2018, the Subcommittee held a hearing to examine efforts to combat seasonal flu, develop a more effective flu vaccine, and prepare a long-term strategy to improve

⁸⁶ CDC, *National Pandemic Influenza Plans* (last reviewed Jun. 15, 2017), available at <https://www.cdc.gov/flu/pandemic-resources/planning-preparedness/national-strategy-planning.html>.

⁸⁷ Letter from the Hon. Greg Walden, Chairman, H. Comm. on Energy & Commerce, *et al.*, to Hon. Thomas Price, M.D., Sec’y, HHS (Apr. 20, 2017), available at <https://archives-energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/documents/20170420HHS.pdf>. In response to Questions for the Record from the Subcommittee’s November 2015 hearing on seasonal influenza, HHS told the Committee that it expected to release the updated plan by the end of 2016. *Id.*

⁸⁸ CDC, *National Pandemic Influenza Plans* (last updated Jun. 15, 2017), available at <https://www.cdc.gov/flu/pandemic-resources/planning-preparedness/national-strategy-planning.html>.

⁸⁹ HHS, *HHS Pandemic Influenza Plan*, at 2 (Nov. 2005), available at <http://www.flu.gov/planning-preparedness/federal/hhspandemicinfluenzaplan.pdf>.

⁹⁰ HHS, *Pandemic Influenza Plan, 2017 Update* (Jun. 2017), available at <https://www.cdc.gov/flu/pandemic-resources/pdf/pan-flu-report-2017v2.pdf>.

⁹¹ *Id.* at 11.

⁹² Hearing before the U.S. House of Reps., Energy and Commerce Subcommittee on Oversight and Investigations, *U.S. Public Health Preparedness for Seasonal Influenza: Has the Response Improved?*, 114th Cong. (Nov. 19, 2015).

seasonal flu preparedness. Then-Commissioner of the FDA Dr. Scott Gottlieb testified that FDA scientists were looking at data “to look for differences in effectiveness in those receiving egg-based and cell-based vaccines, as well as differences in effectiveness in those who were vaccinated with standard-dose versus high-dose influenza vaccine and adjuvanted influenza vaccine.”⁹³ Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases (NIAID) at NIH, testified that NIAID “has made the development of universal influenza vaccines a high priority, and in this regard, has begun a concerted effort to galvanize research in the field.”⁹⁴

Also at the March 2018 hearing, Dr. Rick A. Bright described BARDA’s unique role in making vaccines for both pandemic and seasonal flu, stating:

BARDA also established the first and largest pre-pandemic influenza vaccine stockpile in the world, one that could, if necessary, vaccinate tens of millions in the event of H5N1 and has advanced science of antigens and adjuvants through unique programs. The stockpile and rapid response capability is a true national asset that not only provides vaccine to America’s first responders and critical workforce, but also provides each vaccine manufacturer that holds a U.S. license with valuable lead time to develop vaccines against influenza viruses that pose the greatest risk to becoming a pandemic virus.⁹⁵

On September 19, 2019, the President issued an Executive Order (EO) entitled *Modernizing Influenza Vaccines in the United States to Promote National Security and Public Safety*.⁹⁶ The EO:

[D]irects actions to reduce the United States’ reliance on egg-based influenza vaccine production; to expand domestic capacity of alternative methods that allow more agile and rapid responses to emerging influenza viruses; to advance the development of new, broadly protective vaccine candidates that provide more effective and longer lasting immunities; and to support the promotion of increased influenza vaccine immunization across recommended populations.⁹⁷

In addition, the EO also established a National Influenza Vaccine Task Force in order to identify actions to achieve the EO’s objectives, as well as monitor and report on the implementation and results of those actions.

⁹³ Hearing before the U.S. House of Reps., Energy and Commerce Subcommittee on Oversight and Investigations, *Examining U.S. Public Health Preparedness for and Response Efforts to Seasonal Influenza*, 115th Cong. (Mar. 8, 2018).

⁹⁴ *Id.*

⁹⁵ *Id.*

⁹⁶ The White House, *Executive Order on Modernizing Influenza Vaccines in the United States to Promote National Security and Public Health* (Sept. 19, 2019), available at <https://www.whitehouse.gov/presidential-actions/executive-order-modernizing-influenza-vaccines-united-states-promote-national-security-public-health/>.

⁹⁷ *Id.*